

### **REMARKS**

Claims 54-63 are pending, claims 60-63 being withdrawn.

#### **Sequence Listing**

The Examiner has indicated that the sequences in Figure 27 of the application are not followed by a sequence identifier and were not included in the Sequence Listing submitted with the application as filed on April 7, 2004. Applicants respectfully assert that this is incorrect.

As pointed out in Applicants Response to Restriction Requirement dated April 21, 2005, the following documents were submitted with the filing of the above-identified application:

- ❖ Preliminary Amendment under 37 C.F.R. § 1.121 And Submission of Sequence Listing
- ❖ Statement to Support Filing and Submission of Sequence Listing In Accordance with 37 C.F.R. § 1.821-1.825
- ❖ Sequence Listing

A copy of these documents with the postcard indicating receipt of them on April 7, 2004 is enclosed for the convenience of the Examiner.

Applicants Preliminary Amendment amended the description of Figure 27 in the Brief Description of the Drawing to include the sequence identifiers for the two peptides references in the figure. Additionally, as can be seen in the attached Sequence Listing, SEQ ID NO. 2, which corresponds to H-H-H-H-H-H as used in Figure 27, and SEQ ID NO. 3, which corresponds to R-R-R-R-R-R as used in Figure 27, were included in the Sequence Listing submitted with the application when filed.

Thus, Applicants assert that the pending application is in compliance with the requirements of 37 C.F.R. §§ 1.821-1.825 and respectfully request that the Examiner acknowledge such compliance.

#### **Election of Invention**

The Examiner has issued a restriction requirement alleging that the application claims two distinct inventions. Specifically, the Examiner identifies the two inventions as being:

- ❖ Group I, consisting of claims 54-59, drawn to a method for identifying a ligand that binds to a protein, classified in Class 436, subclass 89; and

- ❖ Group II, consisting of claims 60-63, drawn to a computer program product, classified in Class 702, subclass 19.

Pursuant to 37 C.F.R. §1.142, Applicants elect Group I, claims 54-59 without traverse. Claims 60-63 are withdrawn from further consideration by the Examiner under 37 C.F.R. 1.142(b), as being drawn to a non-elected invention. Applicants, however, reserve the right pursuant to 35 U.S.C. §121 to file one or more divisional applications directed to the non-elected invention during the pendency of the present application.

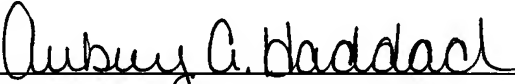
**CONCLUSION**

Applicants respectfully request prompt examination on the merits of the full scope of claims 54-59. As this response is being filed within the one-month shortened statutory period for reply, no fees are believed to be due in connection with this submission. However, if Applicants are incorrect in this assumption, please charge any fee due to Deposit Account No. 23-2415, referencing Docket No. 30923-702.306.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (858) 350-2319.

Respectfully submitted,

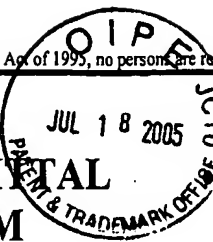
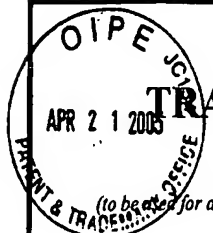
WILSON SONSINI GOODRICH & ROSATI

  
Aubrey Haddach, Reg. No. 48,374

Date: July 18, 2005

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  <p><b>TRANSMITTAL FORM</b></p> <p>(to be used for all correspondence after initial filing)</p>		Application Number	10/821,274
		Filing Date	April 7, 2004
		First Named Inventor	Michael W. PANTOLIANO
		Art Unit	1744
		Examiner Name	David A Reading
Total Number of Pages in This Submission	33	Attorney Docket Number	30923-702.386

**ENCLOSURES (Check all that apply)**

<input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input checked="" type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Response to Missing Parts/Incomplete Application <input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s)	<input type="checkbox"/> After Allowance communication to Technology Center (TC) <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): 1. Copy of Preliminary Amendment, Submission of Sequence Listing, and IDS filed April 7, 2004 2. Itemized Return Postcard
Remarks		

**SIGNATURE OF APPLICANT, ATTORNEY OR AGENT**

Firm or Individual name	Aubrey A. Haddach, Reg. No. 48,374, WILSON SONSINI GOODRICH & ROSATI		
Signature	<i>Aubrey A. Haddach</i>		
Date	April 21, 2005		

**CERTIFICATE OF TRANSMISSION/MAILING**

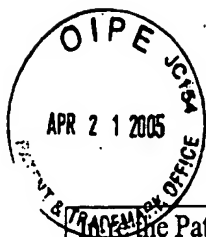
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Typed or printed name	Michael Boyd		
Signature	<i>[Signature]</i>	Date	April 21, 2005

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

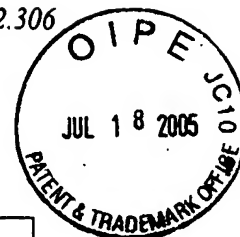
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EV517732768US

WSGR Reference No. 30923-702.306



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



Re: the Patent Application of:

Applicant: Michael W. Pantoliano *et al.*

Serial No.: 10/821,274

Filed: April 7, 2004

Title: MICROPLATE THERMAL SHIFT  
ASSAY APPARATUS FOR LIGAND  
DEVELOPMENT AND MULTI-VARIABLE  
PROTEIN CHEMISTRY OPTIMIZATION

Group Art Unit: 1744

Examiner: David A. Redding

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Michael Boyd**RESPONSE TO RESTRICTION REQUIREMENT**

Mail Stop Amendment  
Commissioner for Patents  
PO Box 1450  
Alexandria, Virginia 22313-1450

Sir:

This is a response to the Office Communication mailed March 21, 2005. No fees are believed to be due in connection with this submission. However, if any fees are required, please charge any fee due to Deposit Account No. 23-2415, Referencing Docket No. 30923-702.306.

**Listing of the Claims**, reflecting the status of the claims, begins on page 2 of this paper.

**Remarks** begin on page 5 of this paper.

**Conclusion** is on page 6 of this paper.

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in this application.

The following amendments do not constitute an admission regarding the patentability of the amended subject matter and should not be so construed. Applicant reserves the right to pursue the subject matter of the canceled claims in this or any other appropriate patent application.

**Listing of Claims:**

Claims 1-53. (Cancelled).

54. (Previously presented) A method for identifying a ligand that binds to a protein, comprising the steps of:

(1) receiving unfolding data that indicates thermal unfolding as a function of temperature for a protein incubated with a molecule tested for binding;

(2) determining an unfolding temperature for the protein in the presence of the molecule from the unfolding data;

(3) comparing the unfolding temperature midpoint for the protein incubated with the ligand with the unfolding temperature midpoint for the protein in the absence of any molecules tested for binding; and

(4) determining that the molecule tested for binding binds to the protein when a difference between the unfolding temperature midpoint for the protein in the presence of the molecule and unfolding temperature midpoint for the protein in the absence of any molecules tested for binding exceeds a threshold.

55. (Previously presented) The method according to claim 54, wherein step (2) comprises the step of plotting thermal unfolding as a function of temperature for the protein incubated with the molecule, and determining the unfolding temperature midpoint for the protein in the presence of the molecule from the plot.

56. (Previously presented) The method according to claim 55, further comprising the steps of:

(5) receiving data that indicates thermal unfolding as a function of temperature for the protein in the absence of any molecules tested for binding;

(6) plotting thermal unfolding as a function of temperature for the protein in the absence of any molecules tested for binding; and

(7) determining the unfolding temperature midpoint for the protein in the absence of any molecules tested for binding from the associated plot.

57. (Previously presented) The method according to claim 54, wherein the molecule that binds is a ligand, and further comprising the step of:

(5) estimating ligand binding affinity.

58. (Previously presented) The method according to claim 57, wherein step (5) comprises the step of estimating the ligand binding affinity at the unfolding temperature midpoint.

59. (Previously presented) The method according to claim 54, wherein step (1) comprises the step of receiving fluorescence data.

60. (Previously presented) A computer program product comprising a computer useable medium having control logic embodied in said medium, for causing a computer to process thermal unfolding data, said control logic comprising:

a thermal unfolding data generating routine that causes the computer system to generate thermal unfolding data from fluorescence information received from a plurality of samples;

a thermal unfolding curve generation routine that causes the computer system to generate thermal curves from the thermal unfolding data; and

a thermal unfolding curve comparison routine that causes the computer system to compare the thermal unfolding curves.

61. (Previously presented) A computer program product comprising a computer useable medium having control logic embodied in said medium, for causing a computer to process thermal unfolding data, said control logic comprising:

a thermal unfolding data generating routine that causes the computer system to generate thermal unfolding data from fluorescence information received from a plurality of samples;

a thermal midpoint determining routine that causes the computer system to determine the thermal unfolding midpoint temperatures from the thermal unfolding data; and

a thermal midpoint comparison routine that causes the computer system to compare the thermal unfolding midpoint temperatures.

62. (Previously presented) The computer program product according to claim 61, wherein said thermal midpoint determining routine comprises a thermal unfolding curve generation routine that causes the computer system to generate thermal curves from the thermal unfolding data and to determine the thermal unfolding temperature midpoints from the curves.

63. (Previously presented) The computer program product according to claim 61, wherein said control logic further comprises:

a positioning control routine that causes the computer system to control a positioning system for the plurality of samples.

**REMARKS**

Claims 54-63 are pending.

With the filing of the above-identified application, Applicants filed the following documents:

- ❖ Preliminary Amendment under 37 C.F.R. § 1.121 And Submission of Sequence Listing
- ❖ Statement to Support Filing And Submission Of Sequence Listing In Accordance with 37 C.F.R. § 1.821-1.825.
- ❖ Request to Approve Proposed Drawing Corrections
- ❖ Information Disclosure Statement and Form PTO-1449

A copy of these documents with the postcard indicating receipt of them on April 7, 2004 is enclosed for your convenience. Because the April 7<sup>th</sup> Preliminary Amendment cancelled claims 1-53 and added new claims 54-63, Applicants respectfully assert that the Restriction Requirement is improper with respect to the pending claims.

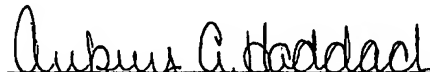
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CONCLUSION

Applicants respectfully request prompt examination on the merits of the full scope of claims 54-63. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (858) 350-2319.

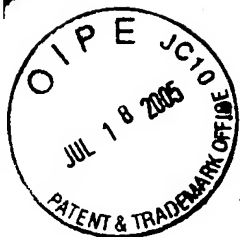
Respectfully submitted,

WILSON SONSINI GOODRICH & ROSATI

  
Aubrey Haddach, Reg. No. 48,374

Date: April 21, 2005

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Palo Alto, CA 94304  
(858) 350-2319  
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**PAT-103 5/02 PTO RECEIPT FOR INDICATED ITEMS**

Atty/Agent: Aubrey A. Haddach

Application No.: Not yet assigned

Date: 04-07-04

Applicant/Inventor(s): Pantoliano et al.

C# 044988

Title: Microplate Thermal Shift Assay Apparatus for Ligand  
Development and Multi-Variable Protein Chemistry Optimization

M# 0308977

ENCLOSED: EL 989434393 US

☐ Response to Office Action ☐ Amendment ☐ Appendix ☐ Transmittal

☒ New Patent Application ☐ Request for PCT # \_\_\_\_\_ No. of Pages

# 1 No. of Pages Abstract; # 109 No. of Pages Spec & Claims

# 42 No. Sheets Drawings (Fig(s) 1 to 42 ) ☐ 1 set Formal

☒ Declaration (3 #pgs) ☐ Issue and Printing Fees ☐ Certificate of Correction

☐ Assignment ☐ PCT Power of Attorney ☐ Change of Entity Status

# \_\_\_\_\_ No. of Priority Documents ☐ Response to Invitation to Correct Defects

☐ PCT Fee Calculation Sheet (in duplicate) ☐ Petition for Extension of Time

☒ IDS # 5 No. of Pages ☐ cited Appl(s). ☐ Foreign sch rept./OA

☒ PTO-1449 ☒ cited docs. ☐ Status Letter

Other: Statement to Support Filing and Submission of Sequence Listing; Electronic Copy of  
Sequence Listing; Request to Approve Proposed Drawing Corrections; Preliminary Amendment  
and Submission of Sequence Listing; Return Post Card

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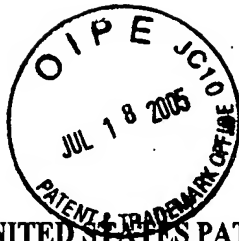
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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

<p>In re the Patent Application of:</p> <p>Applicant: Pantoliano <i>et al.</i></p> <p>Serial No.: Not yet assigned</p> <p>Filed: April 7, 2004</p> <p>Title: <i>Microplate Thermal Shift Assay Apparatus For Ligand Development And Multi-Variable Protein Chemistry Optimization</i></p>	<p>Group Art Unit: Not yet assigned</p> <p>Examiner: Not yet assigned</p> <hr/> <p><u>Certificate of Mailing Under C.F.R. §1.8</u></p> <p>I hereby certify that this correspondence and all marked attachments are being deposited by Express Mail, Express Mailing Label No.: EL 989434393 US on April 7, 2004 addressed to: Mail Stop Patent Application, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.</p> <p>By:  Abigail Rivamonte</p>
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**PRELIMINARY AMENDMENT UNDER 37 C.F.R. § 1.121**  
**AND SUBMISSION OF SEQUENCE LISTING**

MAIL STOP PATENT APPLICATION  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

The above-identified application, enclosed herewith, is filed under 37 C.F.R. § 1.53(b) as a continuing (continuation) application during pendency of parent application Serial No. 09/801,676. Prior to examination of this application and before calculations of the fees, Applicants respectfully request the that following amendments be entered:

Amendments to the Specification are reflected on page 2 of this paper.

Amendments to the Drawings are reflected on page 4 of this paper.

Amendments to the Claims are reflected in the listing of claims which begins on page 5 of this paper.

Remarks begin on page 8 of this paper.

Conclusion begins on page 9 of this paper.

**Amendment to the Specification:**

Please amend the specification in accordance with the following:

Delete the paragraph on page 1, beginning on line 4, and replace it with the following paragraph:

---  
This application is a continuation of co-pending U.S. patent application number 09/801,676, filed March 9, 2001. U.S. patent application number 09/801,676 was filed as a continuation of U.S. patent application number 09/459,996, filed December 14, 1999 (U.S. Patent 6,214,293). U.S. patent application number 09/459,996 was filed as a continuation of 08/853,459, filed May 9, 1997 (U.S. Patent 6,903,920), which claimed priority to U.S. provisional application number 60/017,860, filed May 9, 1996, all of which are incorporated herein by reference in their entireties.

---  
Amend the paragraph on page 17 beginning on line 7, as follows:

---  
Figures 8A and 8B show shows the results of a miniaturized microplate thermal shift assay of aprosulate binding to the D(II) domain of human FGF receptor 1.

---  
Amend the first paragraph on page 5 as shown below:

---  
Like calorimetric technologies, spectral technologies have been used to monitor temperature induced protein unfolding (Bouvier, M. *et al.*, *Science* 265:398-402 (1994); Chavan, A.J. *et al.*, *Biochemistry* 33:7193-7202 (1994); Morton, A. *et al.*, *Biochemistry* 1995:8564-8575 (1995)). ~~The calorimetric and spectral thermal shift studies described above all share a common limitation. In each study, only one binding reaction was heated and assayed at a time. The~~ single sample heating and assay configuration, as conventionally performed, has impeded the application of thermal shift technologies to high throughput screening of combinatorial libraries. Thus, there is a need for a thermal shift technology which can be used to screen combinatorial libraries, can be used to identify an drank lead compounds, and is applicable to all receptor proteins.

Amend the paragraph starting on page 70, line 4, and ending on page 70, line 15, as shown below:

Using the computer controlled process DirectedDiversity® (see U.S. Patent Number 5,463,564), scientists at 3-Dimensional Pharmaceuticals, Inc. have generated a combinatorial library of compounds directed at the active site of human  $\alpha$ -thrombin. Approximately 400 compounds were synthesized and assayed by a conventional spectrophotometric kinetic assay in which succinyl – Ala-Ala-Pro-Arg-p-nitroanilide (SEQ ID NO:1) (Bachem, King of Prussia, PA) served as the substrate. Five of these compounds, which are characterized by  $K_i$ 's that span almost four orders of magnitude in binding affinity, were used to test the range and limits of detection of the thermal shift assay. These five proprietary compounds are listed in Table 3, along with the  $K_i$  for each respective compound, as measured by the kinetic assay (last column).  $K_i$ 's for these compounds ranged from 7.7 nM for 3dp-4026 to 20.0  $\mu$ M for 3dp-3811.

Amend the current version of the paragraph starting on page 19, line 1, and ending on page 19, line 2, to read:

**Figure 27** is a schematic diagram of a method of screening biochemical conditions that optimize protein folding. This method employs denatured protein tagged with H-H-H-H-H (SEQ ID NO: 2) or R-R-R-R-R (SEQ ID NO: 3).

Please insert the sequence listing at the end of the application.

**Amendments to the Drawings:**

Please make the following amendments to the drawings:

---  
Replace FIG. 8 with FIGS. 8A and 8B, as shown in the drawings submitted with the concurrently filed Request to Approve Proposed Drawing Corrections.

---  
Amend FIGS. 25 and 41A as shown in red in the drawings submitted with the concurrently filed Request to Approve Proposed Drawing Corrections.

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**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in this application.

The following amendments do not constitute an admission regarding the patentability of the amended subject matter and should not be so construed. Applicant reserves the right to pursue the subject matter of the canceled claims in this or any other appropriate patent application.

Claims 1-53 have been cancelled. Claims 54-63 have been added. These amendments introduce no new matter and their entry is respectfully requested.

**Listing of Claims:**

Claims 1-53. (Cancelled).

54. (New) A method for identifying a ligand that binds to a protein, comprising the steps of:

(1) receiving unfolding data that indicates thermal unfolding as a function of temperature for a protein incubated with a molecule tested for binding;

(2) determining an unfolding temperature for the protein in the presence of the molecule from the unfolding data;

(3) comparing the unfolding temperature midpoint for the protein incubated with the ligand with the unfolding temperature midpoint for the protein in the absence of any molecules tested for binding; and

(4) determining that the molecule tested for binding binds to the protein when a difference between the unfolding temperature midpoint for the protein in the presence of the molecule and unfolding temperature midpoint for the protein in the absence of any molecules tested for binding exceeds a threshold.

55. (New) The method according to claim 54, wherein step (2) comprises the step of plotting thermal unfolding as a function of temperature for the protein incubated with the molecule, and determining the unfolding temperature midpoint for the protein in the presence of the molecule from the plot.

56. (New) The method according to claim 55, further comprising the steps of:

(5) receiving data that indicates thermal unfolding as a function of temperature for the protein in the absence of any molecules tested for binding;

(6) plotting thermal unfolding as a function of temperature for the protein in the absence of any molecules tested for binding; and

(7) determining the unfolding temperature midpoint for the protein in the absence of any molecules tested for binding from the associated plot.

57. (New) The method according to claim 54, wherein the molecule that binds is a ligand, and further comprising the step of:

(5) estimating ligand binding affinity.

58. (New) The method according to claim 57, wherein step (5) comprises the step of estimating the ligand binding affinity at the unfolding temperature midpoint.

59. (New) The method according to claim 54, wherein step (1) comprises the step of receiving fluorescence data.

60. (New) A computer program product comprising a computer useable medium having control logic embodied in said medium, for causing a computer to process thermal unfolding data, said control logic comprising:

a thermal unfolding data generating routine that causes the computer system to generate thermal unfolding data from fluorescence information received from a plurality of samples;

a thermal unfolding curve generation routine that causes the computer system to generate thermal curves from the thermal unfolding data; and

a thermal unfolding curve comparison routine that causes the computer system to compare the thermal unfolding curves.

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61. (New) A computer program product comprising a computer useable medium having control logic embodied in said medium, for causing a computer to process thermal unfolding data, said control logic comprising:

a thermal unfolding data generating routine that causes the computer system to generate thermal unfolding data from fluorescence information received from a plurality of samples;

a thermal midpoint determining routine that causes the computer system to determine the thermal unfolding midpoint temperatures from the thermal unfolding data; and

a thermal midpoint comparison routine that causes the computer system to compare the thermal unfolding midpoint temperatures.

62. (New) The computer program product according to claim 61, wherein said thermal midpoint determining routine comprises a thermal unfolding curve generation routine that causes the computer system to generate thermal curves from the thermal unfolding data and to determine the thermal unfolding temperature midpoints from the curves.

63. (New) The computer program product according to claim 61, wherein said control logic further comprises:

a positioning control routine that causes the computer system to control a positioning system for the plurality of samples.

### **REMARKS**

This Preliminary Amendment is being submitted with the filing of the above-identified application, and therefore Applicants believe that this response is timely filed, and that no fees are due in connection with this submission. In the event that Applicants are incorrect in their assumption, please charge any fee due in connection with this submission to Deposit Account No. 50-2212, Order Number 044988.030.8977.

#### ***Amendments to the Specification***

The specification has been amended to direct the entry of the enclosed sequence listing after the claims of the above-identified application and to provide SEQ ID NOs next to the specific sequences. In accordance with 37 C.F.R. § 1.821(e), a computer readable copy of the sequence listing is included herewith. In accordance with 37 C.F.R. § 1.821(f), the paper copy of the sequence listing and the computer readable copy of the sequence listing submitted herewith in the above application are the same.

The amendments to the Specification are made in accordance with similar amendments in the parent case. These amendments introduce no new matter. Thus, Applicants respectfully request that the sequence listing submitted herewith be introduced into the above-identified application.

#### ***Amendments to the Drawings***

FIG. 8 is replaced with FIGS. 8A and 8B, as shown in the drawings submitted with the concurrently filed Request to Approve Proposed Drawing Corrections. Similar changes were approved by the Examiner in the parent application (Serial No. 09/801,676).

FIGS. 25 and 41A are amended as shown in red in the drawings submitted with the concurrently filed Request to Approve Proposed Drawing Corrections. Specifically, in FIG. 25, a diamond symbol and the text "pH 8/0.1 NaCl" is sought to be added and in FIG. 41A, the legend "Control ANS/No Protein" is sought to be added. Similar amendments were approved by the Examiner in the parent application (Serial No. 09/801,676).

The proposed changes add no new matter to the application. Applicants request that the Examiner approve the proposed corrections. After official communication of such approval, Applicants will make the appropriate corrections and submit revised formal drawings.

*Amendments to the Claims*

Newly added claims 54-63 are directed to data processing aspects of the present invention. Support for claims 54-63 can be found throughout the specification, for example, at page 67, line 1 through page 69, line 9, and Figures 37, 40, and 42.

Claims 54-63 substantially correspond to claims 54-58, 65, and 67-70 from the parent application (Serial No. 09/801,676). Claims 60-63 substantially correspond to non-elected claims 80-83 from the grandparent application (Serial No. 09/459,996, which issued as U.S. Patent No. 6,214,293).

Newly added claims are believed to introduce no new matter and their entry is respectfully requested.

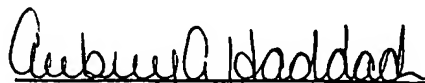
**CONCLUSION**

Applicants respectfully request that the proposed amendment be entered and the claims examined on the merits. Early and favorable consideration is requested.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

Date: April 7, 2004

  
Aubrey A. Haddach  
Registration No. 48,374  
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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re the Patent Application of:

Applicant: Pantoliano *et al.*

Serial No.: Not yet assigned

Filed: April 7, 2004

Title: *Microplate Thermal Shift Assay  
Apparatus For Ligand Development  
And Multi-Variable Protein Chemistry  
Optimization*

Group Art Unit: Not yet assigned

Examiner: Not yet assigned

Certificate of Mailing Under C.F.R. §1.8

I hereby certify that this correspondence and all marked attachments are being deposited by Express Mail, Express Mailing Label No.: EL 989434393 US on April 7, 2004 addressed to: Mail Stop Patent Application, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

By: *A. Rivamonte*  
Abigail Rivamonte

COPY

**STATEMENT TO SUPPORT FILING AND SUBMISSION OF SEQUENCE LISTING  
IN ACCORDANCE WITH 37 C.F.R. §1.821-1.825**

**MAIL STOP PATENT APPLICATION**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

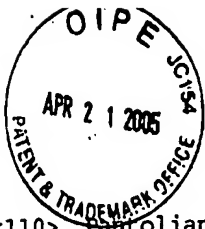
I hereby state that the content of the paper and computer readable copies of the Sequence Listing, submitted in accordance with 37 C.F.R. § 1.821(c), (e), (f) and (g), or § 1.825(d) and (b), respectively, are the same.

Respectfully submitted,

Date: April 7, 2004

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SEQUENCE LISTING



<110> Pantoliano, Michael W.  
Bone, Roger F.  
Rhind, Alexander W.  
Salemme, Francis R.

<120> Computer Program for Thermal Shift Assay Apparatus for  
Ligand Development and Multi-Variable Protein Chemistry Optimization

<130> 044988-0308977

<140> To be assigned

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<151> 1996-05-09

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<151> 2001-03-09

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